

Amendments to the Claims:

All amendments and cancellations to the claims are made without prejudice or disclaimer. This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Original) A method of evaluating a compound for a modulatory effect on a disorder, the method comprising:

- a) providing a library of compounds;
- b) contacting each compound of the library to a GH/IGF-1 axis component or a functional fragment thereof, *in vitro*;
- c) evaluating interaction between each compound and the GH/IGF-1 axis component;
- d) selecting a subset of compounds from the library based on the evaluated interactions;
- e) contacting a compound of the subset to (i) a cell *in vitro*, the cell being from a subject having the disorder or from non-human animal model of the disorder, or (ii) a non-human animal model of the disorder; and
- f) evaluating the cell or the animal model, wherein a change in an parameter of the disorder identifies the respective compound as having a modulatory effect on the disorder.

2. (Original) The method of claim 1 wherein contacting the compound to the animal model comprises administering the compound to the animal model.

3. (Original) The method of claim 1 wherein the disorder is a neoplastic disorder, a neurological disorder, other than a disorder caused by polyglutamine aggregation, a metabolic

disorder, an immunological disorder, a tissue repair condition, a dermatological disorder, a dermatological tissue condition, or a cardio-vascular disorder.

4. (Original) The method of claim 1 wherein the disorder is Alzheimer's, Parkinson's, ALS, skeletal muscle atrophy, multiple sclerosis, a neuropathy, age-related macular degeneration, diabetic retinopathy, or non-insulin-dependent diabetes.

5. (Original) The method of claim 1 wherein the component is a cell surface receptor or secreted molecule.

6. (Original) A method of evaluating a compound for a modulatory effect on a disorder, the method comprising:

- a) selecting a GH/IGF-1 axis modulator;
- b) contacting the modulator to (i) a cell in vitro, the cell being from a subject having the disorder or from non-human animal model of the disorder, or (ii) a non-human animal model of the disorder; and
- c) evaluating the cell or the animal model, wherein a change in an parameter of the disorder identifies the respective compound as having a modulatory effect on the disorder, wherein the disorder is selected from the group consisting of: an immunological disorder, a dermatological disorder, a dermatological tissue condition, a cardio-vascular disorder, or a neurological disorder, other than a neurological disorder caused by polyglutamine aggregation.

7. (Original) The method of claim 6 wherein the modulator is a compound that directly antagonizes a positively acting GH/IGF-1 axis component.

8. (Original) The method of claim 6 wherein the modulator is a compound that directly agonizes an inhibitory GH/IGF-1 axis component.

9. (Original) A method of evaluating a compound for a modulatory effect on life span regulation or potential, the method comprising

- a) providing a test compound;
- b) contacting the test compound to a GH/IGF-1 axis component *in vitro*;
- c) evaluating interaction between the test compound and the GH/IGF-1 axis component;
- d) administering the test compound to an adult, non-human subject; and
- e) evaluating an age-associated parameter of the adult subject, wherein an interaction between the test compound the GH/IGF-1 axis component and modulation of the age-associated parameter relative to a control subject identifies the respective compound as having a modulatory effect on lifespan regulation or potential.

10. (Original) A method of evaluating a compound for a modulatory effect on life span regulation or potential, the method comprising

- a) providing a library of compounds;
- b) contacting each compound of the library to a GH/IGF-1 axis component *in vitro*;
- c) evaluating interaction between each compound and the GH/IGF-1 axis component;
- d) selecting a subset of compounds from the library based on the evaluated interactions;
- e) administering (e.g., individually) each compound of the subset to an adult, non-human subject; and
- f) evaluating an age-associated parameter of the adult subject, wherein modulation of the age-associated parameter relative to a control subject identifies the respective compound as having a modulatory effect on lifespan regulation or potential.

11. (Original) The method of claim10, wherein the age-associated parameter comprises one or more of:

- (i) lifespan of the subject, or a cell in the subject;
- (ii) presence or abundance of a gene transcript or gene product that has a biological age-dependent expression pattern in a cell of the subject;

- (iii) resistance of the subject or a cell of the subject to stress;
- (iv) one or more metabolic parameters of the subject or a cell of the subject ; and
- (v) proliferative capacity of a cell of the subject.

12. (Original) The method of claim10, wherein the *in vitro* contacting is a cell-based assay.

13. (Original) The method of claim10, wherein the *in vitro* contacting is a cell-free assay.

14. (Original) The method of claim10, wherein the adult subject is a non-human mammal.

15. (Original) The method of claim10, wherein the subject has normal IGF-1 levels.

16. (Original) The method of claim10, the GH/IGF-1 axis component is a cell surface receptor.

17. (Original) The method of claim10, the GH/IGF-1 axis component is a pre-IGF1 component.

18. (Original) The method of claim10, the GH/IGF-1 axis component is a post-IGF1 component.

19. (Original) The method of claim 10 wherein the library comprises multiple compounds that have a molecular weight less than 7000 Daltons.

20. (Original) The method of claim 10 wherein the library comprises one or more of an immunoglobulin, a peptide, a nucleic acid aptamer, a dsRNA, a siRNA, a ribozyme, or an antisense nucleic acid.

21. (Original) The method of claim 10 wherein each compound of the library is non-polymeric.

22. (Original) The method of claim 10 further comprising formulating an identified compound as a pharmaceutical composition.

23. (Original) A method of evaluating a compound for a modulatory effect on life span regulation or potential, the method comprising

- a) providing a test compound;
- b) contacting the test compound to a GH/IGF-1 axis component *in vitro*;
- c) evaluating interaction between the test compound and the growth hormone/IGF-1 axis component;
- d) contacting the test compound to a cell; and
- e) evaluating an age-associated parameter of the cell, wherein an interaction between the test compound the GH/IGF-1 axis component and modulation of the age-associated parameter relative to a control cell identifies the respective compound as having a modulatory effect on lifespan regulation or potential.

24. (Original) The method of claim 23, wherein the age-associated parameter comprises one or more of:

- (i) lifespan of the cell;
- (ii) presence or abundance of a gene transcript or gene product that has a biological age-dependent expression pattern in the cell;
- (iii) resistance of the cell to stress;

- (iv) one or more metabolic parameters of the cell ;
- (v) proliferative capacity of the cell ; and
- (vi) physical appearance or behavior of the cell.

25. (Original) A method identifying a GH/IGF-1 axis antagonist or partial agonist, the method comprising

a) providing a test compound that is obtained by chemically modifying an agonist of a GH/IGF-1 axis component or that is selected for structural similarity to an agonist of a GH/IGF-1 axis component; and

b) evaluating a property of a GH/IGF-1 axis component *in vitro*, in a cell, or in an organism in the presence of the test compound, wherein ability of the test compound to modulate the property of the GH/IGF-1 axis component identifies the test compound as a GH/IGF-1 axis antagonist.

26. (Original) The method of claim 25 wherein the evaluating comprises a cell-free assay or a cell-based assay.

27. (Original) The method of claim 25 wherein the evaluating comprises administering the test compound to an adult organism.

28. (Original) The method of claim 27 wherein the organism has normal IGF-1 levels prior to the administering.

29. (Original) The method of claim 27 wherein a cohort of adult organism are treated and evaluated, each organism of the cohort characterized by normal IGF-1 levels prior to the treating.

30. (Original) The method of claim 27 wherein the evaluating comprises evaluating GH or IGF-1 levels, and decreased levels of growth hormone and/or IGF-1 identifies the test compound as an agent as a modulator.

31. (Original) The method of claim 27 wherein the evaluating comprises evaluating activity of an GH/IGF-1 axis component in the organism.

32. (Original) The method of claim 25 further comprising d) evaluating an age-associated parameter of a subject treated with the test compound, wherein modulation the age-associated parameter relative to a control subject further identifies the test compound as an agent that modulates lifespan regulation or potential.

33. (Original) A method of identifying an agent that modulates lifespan regulation of an adult animal, the method comprising

- a) selecting an agent that alters a property of GH/IGF-1 axis;
- b) administering the agent to a subject; and
- c) evaluating an age-associated parameter in the subject, wherein modulation of the age-associated parameter identifies the agent as an agent that modulates lifespan regulation or potential.

34. (Original) The method of claim 33 wherein the agent is a direct antagonist of a positively acting component of the GH/IGF-1 axis.

35. (Cancelled)

36. (New) The method of claim 25, wherein the test compound is combined with a pharmaceutically acceptable carrier.